

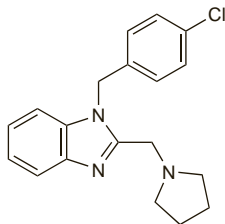
**Clemizole Hydrochloride** (BANM, rINNM)

AL-20; Clémizole, Chlorhydrate de; Clemizoli Hydrochloridum; Hidrocloruro de clemizol. 1-(4-Chlorobenzyl)-2-(pyrrolidin-1-yl-methyl)benzimidazole hydrochloride.

Клемизола Гидрохлорида

$C_{19}H_{20}ClN_3 \cdot HCl = 362.3$ .

CAS — 442-52-4 (clemizole); 1163-36-6 (clemizole hydrochloride).



(clemizole)

**Profile**

Clemizole hydrochloride is a sedating antihistamine (p.561). It has been used for the symptomatic relief of allergic conditions, in pruritic skin disorders, and in combination preparations for the treatment of symptoms of the common cold. Clemizole has also been applied topically as the hexachlorophene, the sodium sulfate, and the undecylate derivatives in topical and rectal preparations combined with corticosteroids and local anaesthetics, although as with other antihistamines, there is a risk of sensitisation.

See p.251 for the use of clemizole penicillin.

**Preparations**

**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** Arg.: Apracur†; Braz.: Ultraproct; Hong Kong: Ultraproct†; Indon.: Ultraproct; Thai.: Apracur; Scheriproct†.

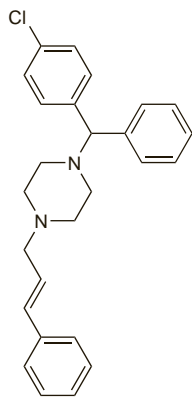
**Clocinazine Hydrochloride** (rINNM)

Chlorcinnazine Dihydrochloride; Clocinazine, Chlorhydrate de; Clocinazini Hydrochloridum; Hidrocloruro de clocinazina. 1-(4-Chlorobenzhydryl)-4-cinnamylpiperazine dihydrochloride.

Клоциназина Гидрохлорида

$C_{26}H_{27}ClN_2 \cdot 2HCl = 475.9$ .

CAS — 298-55-5 (clocinazine).



(clocinazine)

**Profile**

Clocinazine hydrochloride, a piperazine derivative, is an antihistamine (p.561) given by mouth in combination preparations for the symptomatic treatment of upper respiratory-tract disorders, often with a decongestant.

**Preparations**

**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** Fr.: Denoral†; Ital.: Denoral†; Spain: Senioral.

**Cyclizine** (BAN, rINN)

Ciclizina; Cyclizinum; Cykлизин; Sikлизин; Syklitsiini. 1-Benzhydryl-4-methylpiperazine.

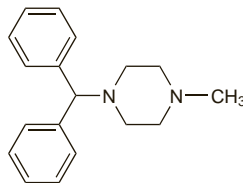
Циклизин

$C_{18}H_{22}N_2 = 266.4$ .

CAS — 82-92-8.

ATC — R06AE03.

ATC Vet — QR06AE03.

**Pharmacopoeias.** In Br:

**BP 2008** (Cyclizine). A white or creamy white, crystalline powder. Practically insoluble in water. It dissolves in most organic solvents and in dilute acids. M.p. about 107°. A saturated solution in water has a pH of 7.6 to 8.6.

**Cyclizine Hydrochloride** (BANM, rINNM)

Cikлизин-hidroklorid; Cikлизино hidrokloridas; Cyclizine, chlorhydrate de; Cyclizini hydrochloridum; Cykлизин hydrochlorid; Cyclizinihydroklorid; Hidrocloruro de ciclizina; Syklitsiinihydrokloridi.

Циклизина Гидрохлорида

$C_{18}H_{22}N_2 \cdot HCl = 302.8$ .

CAS — 303-25-3.

ATC — R06AE03.

ATC Vet — QR06AE03.

**Pharmacopoeias.** In Eur. (see p.vii) and US.

**Ph. Eur. 6.2** (Cyclizine Hydrochloride). A white or almost white, crystalline powder. Slightly soluble in water and in alcohol. A 2% solution in alcohol 2 vol. and water 3 vol. has a pH of 4.5 to 5.5. Protect from light.

**USP 31** (Cyclizine Hydrochloride). A white, odourless, crystalline powder or small colourless crystals. Soluble 1 in 115 of water and of alcohol and 1 in 75 of chloroform; insoluble in ether. pH of a 2% solution in alcohol 2 vol. and water 3 vol. is between 4.5 and 5.5. Store in airtight containers. Protect from light.

**Cyclizine Lactate** (BANM, rINNM)

Cyclizine, Lactate de; Cyclizini Lactas; Lactato de ciclizina.

Циклизина Лактат

$C_{18}H_{22}N_2 \cdot C_3H_6O_3 = 356.5$ .

CAS — 5897-19-8.

ATC — R06AE03.

ATC Vet — QR06AE03.

**Pharmacopoeias.** Br. includes an injection of cyclizine lactate.

**Incompatibility.** Cyclizine lactate is reported to be incompatible with oxytetracycline hydrochloride, chlortetracycline hydrochloride, benzylpenicillin, and solutions with a pH of 6.8 or more.

**Cyclizine Tartrate** (BANM, rINNM)

Cyclizine, Tartrate de; Cyclizini Tartras; Tartrato de ciclizina.

Циклизина Тартрат

$C_{18}H_{22}N_2 \cdot C_4H_6O_6 = 416.5$ .

ATC — R06AE03.

ATC Vet — QR06AE03.

**Adverse Effects and Precautions**

As for the sedating antihistamines in general, p.561. Cyclizine may aggravate severe heart failure. Hypotension may occur on injection.

**Abuse.** Cyclizine tablets have been abused either alone or with opioids for their euphoric effects.<sup>1-7</sup> They have been taken by mouth or used to make injections. It has been suggested that cyclizine dependence may occur when it is used with opioids in the treatment of chronic pain.<sup>8</sup>

- Gott PH. Cyclizine toxicity—intentional drug abuse of a proprietary antihistamine. *N Engl J Med* 1968; **279**: 596.
- Kahn A, Harvey GJ. Increasing misuse of cyclizine. *Pharm J* 1985; **235**: 706.
- Atkinson MK. Misuse of cyclizine. *Pharm J* 1985; **235**: 773.
- Halpin D. Misuse of cyclizine. *Pharm J* 1985; **235**: 797.
- Council of the Pharmaceutical Society of Great Britain. Sales of preparations containing cyclizine. *Pharm J* 1989; **84**: 929-34.
- Rubens SM, et al. Cyclizine abuse among a group of opiate dependents receiving methadone. *Br J Addict* 1989; **84**: 929-34.
- Bassett KE, et al. Cyclizine abuse by teenagers in Utah. *Am J Emerg Med* 1996; **14**: 472-4.
- Hughes AM, Coote J. Cyclizine dependence. *Pharm J* 1986; **236**: 130.

**Effects on the blood.** Agranulocytosis occurred in a patient after 6 weeks of treatment with cyclizine 50 mg three times daily.<sup>1</sup> The blood count returned to normal once cyclizine was withdrawn.

1. Collier PM. Agranulocytosis associated with oral cyclizine. *BMJ* 1986; **292**: 174.

**Effects on the heart.** In a study<sup>1</sup> of 11 patients with severe heart failure, cyclizine produced detrimental haemodynamic effects including increased systemic and pulmonary artery pressures and ventricular filling pressures, and negated the vasodilator effects of diamorphine. It was suggested that the use of cyclizine should be avoided in patients with acute myocardial infarction or severe heart failure.

1. Tan LB, et al. Detrimental haemodynamic effects of cyclizine in heart failure. *Lancet* 1988; **i**: 560-1.

**Effects on the liver.** An 8-year-old girl developed jaundice on 2 occasions after taking cyclizine hydrochloride 25 mg daily by mouth. 'Hypersensitivity hepatitis' was considered responsible.<sup>1</sup>

1. Kew MC, et al. 'Hypersensitivity hepatitis' associated with administration of cyclizine. *BMJ* 1973; **2**: 307.

**Pregnancy.** For discussion of the use of antihistamines in pregnancy, including studies involving cyclizine, see p.563.

**Interactions**

As for the sedating antihistamines in general, p.563. Cyclizine may counteract the haemodynamic benefits of opioids (see Effects on the Heart, above) and this should be considered before using preparations that contain a combination of cyclizine and an opioid analgesic.

**General anaesthetics.** For a possible interaction between cyclizine premedication and *barbiturate anaesthetics* see under Thiopental, p.1795.

**Pharmacokinetics**

Cyclizine is absorbed from the gastrointestinal tract and has an onset of action within 2 hours. The duration of action is reported to be about 4 hours. Cyclizine is metabolised in the liver to the relatively inactive metabolite, norcyclizine. Both cyclizine and norcyclizine have plasma elimination half-lives of 20 hours. Less than 1% of the total oral dose is eliminated in the urine in 24 hours.

**Uses and Administration**

Cyclizine, a piperazine derivative, is a sedating antihistamine with antimuscarinic activity, although the sedative effects are not marked.

It is used as an antiemetic in the management of nausea and vomiting (p.564) including motion sickness, postoperative nausea and vomiting, after radiotherapy, and in drug-induced nausea and vomiting. It is included as an antiemetic with some opioids, and in combination preparations for the treatment of migraine attacks (p.616). Cyclizine is also used for the symptomatic treatment of vertigo (p.565) caused by Ménière's disease and other vestibular disturbances.

In the management of nausea and vomiting, cyclizine hydrochloride is given in a usual oral dose of 50 mg up to three times daily, although up to 200 mg may be given in 24 hours if necessary. For the prevention of motion sickness, the first dose should be given about 30 minutes before travelling. Children aged 6 to 12 years may be given 25 mg up to three times daily. Although not licensed in the UK, the *BNFC* suggests that those aged 1 month to 6 years may be given 0.5 to 1 mg/kg (maximum of 25 mg) up to 3 times daily.

Cyclizine is given intramuscularly or intravenously as the lactate. Doses of cyclizine lactate are similar to those of cyclizine hydrochloride given orally. For the prevention of postoperative nausea and vomiting the first dose of cyclizine lactate should be given about 20 minutes before the anticipated end of surgery.

Although not licensed in the UK, cyclizine is also available as suppositories on a named-patient basis. The *BNFC* suggests that children aged 2 to 6 years may be given rectal doses of 12.5 mg; those aged 6 to 12 years, 25 mg; and those aged 12 to 18 years, 50 mg. Doses may be given up to 3 times daily.

Cyclizine salts are used as antiemetics in combination with morphine or dipipanone; the use of such fixed-combination opioid preparations is considered to be